

CLAIMS

1. A method for identifying an anti-streptococcal agent, which method comprises:

- 5 (a) providing, as a first component, an isolated streptococcal M protein or a functional variant thereof;
- (b) providing, as a second component, isolated fibrinogen or a functional variant thereof;
- 10 (c) providing, as a third component, an isolated β_2 integrin or a functional variant thereof;
- (d) contacting said components with a test substance under conditions that would permit the components to interact in the absence of the test substance; and
- (e) determining whether the test substance inhibits the interaction between the components;
- 15 thereby to determine whether a test substance is an anti-streptococcal agent.

2. A method for identifying an anti-streptococcal agent, which method comprises:

- (a) providing, as a first component, a streptococcal M protein or a functional variant thereof;
- 20 (b) providing, as a second component, fibrinogen or a functional variant thereof;
- (c) providing, as a third component, one or more polymorphonuclear neutrophils (PMNs);
- (d) contacting said components with a test substance under conditions that
- 25 would permit the components to interact in the absence of the test substance; and
- (e) monitoring any inhibition of the activation of PMNs;
- thereby to determine whether a test substance is an anti-streptococcal agent.

3. A method according to claim 2 wherein step (d) comprises contacting *S. pyogenes*, fibrinogen and PMNs in the presence of a test substance.

30 4. A method according to claim 2 or 3 wherein inhibition of the activation of PMNs is monitored by measuring the release of heparin binding protein (HBP).

5. A method according to any one of the preceding claims wherein the first component is provided by contacting *Streptococcus pyogenes* with a protease.
6. A method according to claim 5 wherein the protease is derived from a PMN.
7. A method according to claim 5 wherein the protease is endogenous to *S. pyogenes*.
8. A method according to any one of the preceding claims wherein the streptococcal M protein is the M1 protein of *S. pyogenes*, a homologue thereof which maintains the ability to form a complex with fibrinogen, or a functional variant of either thereof which maintains the ability to form a complex with fibrinogen.
9. A method according to claim 8, wherein the functional variant is a fragment of the M1 protein of *S. pyogenes* or a fragment of a homologue thereof.
10. A method according to claim 1, wherein step (e) comprises determining whether the components form aggregates in the presence of the test substance.
11. A test kit suitable for use in identifying a test substance which is capable of inhibiting the interaction between a streptococcal M protein or a functional variant thereof, fibrinogen and a functional variant thereof and a β_2 integrin or a functional variant thereof, which kit comprises:
- (a) an isolated streptococcal M protein or a functional variant thereof;
- (b) isolated fibrinogen or a functional variant thereof; and
- (c) an isolated β_2 integrin or a functional variant thereof.
12. A test kit suitable for use in identifying a test substance which is capable of inhibiting the interaction between a streptococcal M protein or a functional variant thereof, fibrinogen or a functional variant thereof and PMNs, which kit comprises:
- (a) a streptococcal M protein or a functional variant thereof;
- (b) fibrinogen or a functional variant thereof; and
- (c) one or more PMNs.
13. A test kit according to claim 11 or 12 which further comprises one or more buffers.

14. A test kit according to any one of claims 11 to 13 further comprising means for determining whether a test substance disrupts the interaction between the components.

5 15. An anti-streptococcal agent identified by a method according to any one of claims 1 to 10.

16. An anti-streptococcal agent according to claim 15 for use in a method of treatment of the human or animal body by therapy.

17. Use of an integrin antagonist in the manufacture of a medicament for the treatment of a streptococcal infection.

10 18. Use according to claim 17 wherein the antagonist is an anti-integrin antibody, a peptide mimetic or a non-peptide mimetic.

19. Use of an inhibitor of the interaction between streptococcal M protein, fibrinogen and β_2 integrin in the manufacture of a medicament for the treatment of a streptococcal infection.

15 20. Use according to claim 19 wherein the inhibitor is a peptide comprising the sequence GPRP.

21. Use according to claim 19 wherein the inhibitor is an antibody which specifically binds the B-repeats of *S. pyogenes* M1 protein.

20 22. Use of an agent identified by a method according to any one of claims 1 to 10 in the manufacture of a medicament for the treatment of a streptococcal infection.

23. A method of treating an individual suffering from a streptococcal infection comprising administering a therapeutically effective amount of an agent identified by a method according to any one of claims 1 to 10 to a said individual.

25 24. A method of treating an individual suffering from a streptococcal infection comprising administering a therapeutically effective amount of an integrin antagonist to a said individual.

30 25. A method of treating an individual suffering from a streptococcal infection comprising administering a therapeutically effective amount of an inhibitor of the interaction between streptococcal M protein, fibrinogen and β_2 integrin to a said individual.

26. A pharmaceutical composition comprising an inhibitor of the interaction

between streptococcal M protein, fibrinogen and β_2 integrin identified by a method of any one of claims 1 to 10 and a pharmaceutically acceptable carrier or diluent.

27. A method for providing a pharmaceutical composition, which method comprises:

5 (a) identifying an agent that inhibits the interaction between streptococcal M protein, fibrinogen and β_2 integrin by a method according to any one of claims 1 to 10; and

(b) formulating the inhibitor thus identified with a pharmaceutically acceptable carrier or diluent.

10 28. A method of treating an individual suffering from a streptococcal infection, which method comprises:

(a) identifying an agent that inhibits the interaction between streptococcal M protein, fibrinogen and β_2 integrin by a method according to any one of claims 1 to 10; and

15 (b) administering a therapeutically effective amount of the inhibitor thus identified to a said individual.